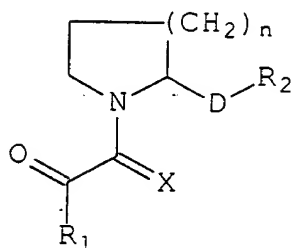


What is claimed is:

1. A compound having the formula (I):



I

5 where

n is 1-3;

X is either O or S;

R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

R₂ is a carboxylic acid or a carboxylic acid isostere; and wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R³ and Z, where

R³ and Z are independently hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, amino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, or CO₂R⁷ where R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl;

or a pharmaceutically acceptable salt, ester, or solvate

thereof;

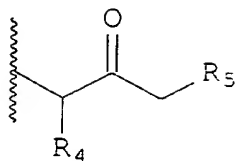
provided that:

when $n=1$, and D is a bond, and R_2 is COOH,

then R_1 is not C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_7 cycloalkyl, C_5-C_7 cycloalkenyl, phenylamine, 2-(3,4-dichlorophenyl)ethyl, hydroxy, ethoxy, benzyl, or Ar_1 , where Ar_1 is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 1-pyridyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, and wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, or Ar_1 are optionally substituted with one or more substituents selected from the group consisting of hydrogen, halo, hydroxyl, nitro, trifluoromethyl, C_1-C_9 straight or branched alkyl, C_2-C_9 straight or branched alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, COOH, and amino;

further provided that:

when $n=1$, and D is a bond, and R_2 is the carboxylic acid isostere $-CONZ(R^3)$, and Z is hydrogen or C_1-C_6 alkyl, and R^3 is phenyl, or C_2-C_6 straight or branched chain alkyl or alkenyl, wherein said alkyl is unsubstituted or substituted in one or more positions with Ar_2 as defined below, C_3-C_8 cycloalkyl, cycloalkyl connected by methyl or a C_2-C_6 straight or branched chain alkyl or alkenyl chain, C_1-C_4 alkyl ester, or Ar_3 where Ar_3 is selected from the group consisting of 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched alkyl, C_2-C_6 straight or branched alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino; wherein said alkyl ester is optionally substituted with phenyl; or R^3 is the fragment:



where R_4 is selected from the group consisting of straight or
 branched chain C_1 - C_6 alkyl optionally substituted with C_3 - C_8
 cycloalkyl, benzyl, or Ar_2 as defined below, and where R_2 is
 5 $COOZ$ or $CONR^6$, where R^6 is selected from the group consisting
 of hydrogen, C_1 - C_6 straight or branched alkyl, and C_2 - C_6
 straight or branched alkenyl, and where R_5 is selected from
 the group consisting of phenyl, benzyl, C_1 - C_6 straight or
 10 branched alkyl, and C_2 - C_6 straight or branched alkenyl, where
 said alkyl or alkenyl is optionally substituted with phenyl;
 then R_1 is not C_1 - C_6 straight or branched chain alkyl, C_2 - C_6
 straight or branched chain alkenyl, substituted thiophene,
 or C_1 - C_4 alkoxy, wherein said alkyl or alkenyl is optionally
 15 substituted in one or more positions with C_3 - C_8 cycloalkyl,
 C_5 - C_7 cycloalkenyl, or Ar_2 , where Ar_2 is defined below, where
 said alkyl, alkenyl, cycloalkyl or cycloalkenyl groups may
 be optionally substituted with C_1 - C_4 alkyl, C_1 - C_4 alkenyl, or
 hydroxy, and where Ar_2 is 1-naphthyl, 2-naphthyl, 2-indolyl,
 20 3-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl,
 3-pyridyl, 4-pyridyl, or phenyl, having one to three
 substituents selected from the group consisting of hydrogen,
 halo, hydroxy, nitro, trifluoromethyl, C_1 - C_6 straight or
 branched alkyl, C_2 - C_6 straight or branched alkenyl, C_1 - C_4
 25 alkoxy, C_2 - C_4 alkenyloxy, phenoxy, benzyloxy, and amino;
 further provided that:

when $n=1$, and X is O , and D is a bond, and R_2 is $-CONH_2$,
 then R_1 is not methyl, ethyl, iso-propyl, iso-butyl, iso-
 pentyl, 4-methylpentyl, indolyl, phenyl, or hydroxyphenyl;
 30 further provided that:

when n=1, and X is O, and D is a bond, and R₂ is cyano, then R₁ is not methyl;

further provided that:

when n=2, and X is O, and D is a bond, and R₂ is CONZ(R³),
5 and R₁ is ethoxy, then R³ or Z is not halo-substituted phenyl;

further provided that:

when n=2, and X is O, and D is a bond, and R₂ is CONZ(R³) and
10 R₁ is substituted thiophene or tetrahydropyranoxy, or methoxy, then R³ or Z is not C₁-C₄ alkyl ester substituted ethyl;

further provided that:

when n=2, and X is O, and D is a bond, and R₂ is CONZ(R³) and
15 R₁ is ethoxy, then R³ or Z is not 4-chlorophenyl;

further provided that:

when n=2, and X is O, and D is a bond, and R₂ is CONZ(R³) and
R₁ is cyclohexyl, then R³ or Z is not ethyl or propyl substituted with phenyl;

further provided that:

20 when D is CH₂, then R₂ is not -OMe, -NHMe, or substituted -NHcyclohexyl;

further provided that:

when D is CH₂, and R₂ is -OH,
then R₁ is not phenyl or pyrrolidinemethanol;

25 further provided that:

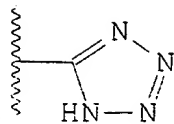
when n=2, and X is O, and D is a bond, and R₂ is COOH,
then R₁ is not methyl, tert-butyl, 1,1-dimethyl-2-methyl-propyl, 1,1-dimethyl-propyl, methoxy, ethoxy, phenyl, tetrahydropyranoxy substituted C₄-C₆ alkyl, 1-methyl-1-methoxyamide, 1-methylcyclohexyl, 3-iodophenyl, 3-methyl ester-cyclopentyl, 1,1-dimethyl-6-phenyl-hex-3,5-dioxy, or trimethoxyphenyl.
30

2. The compound of claim 1, wherein R₂ is a carbocycle or
35 heterocycle containing any combination of CH₂, O, S, or N in

any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R^3 .

3. The compound of claim 1, wherein R_2 is selected from the group consisting of:

Year	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	



Sub
R³
cont.

where the atoms of said ring structure may be optionally substituted at one or more positions with R³.

4. The compound of claim 1, wherein R₂ is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CONZ(R³); -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

Sub
R²
10 5. The compounds, (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinetetrazole; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarbonitrile; and (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-aminocarbonyl piperidine; and
15 compounds 1-25, 27, 28, 31-33, and 35-136 of Tables I, II, and III.

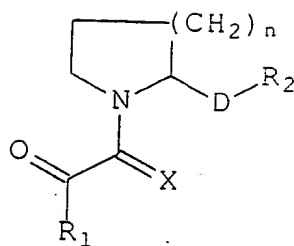
6. The compound 1-(2-[3-(4-Fluorophenyl)(1,2,4-oxadiazol-5-yl)]pyrrolidinyl)-3,3-di-methylpentane-1,2-dione.

20 7. The compound 3,3-Dimehyl-1-[2-(3-methyl(1,2,4-oxadiazol-5-yl))pyrrolidinyl]pentane-1,2-dione.

8. A pharmaceutical composition, comprising:

- 25 a) an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere; and
b) a pharmaceutically acceptable carrier.

Sub
R³
30 9. The pharmaceutical composition of claim 8, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

X is either O or S;

5 R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

10 D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

R₂ is carboxylic acid or a carboxylic acid isostere; and

15 wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R³, where

20 R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate thereof.

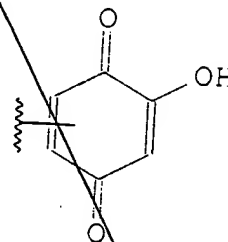
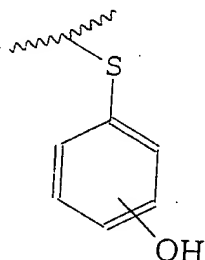
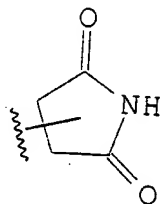
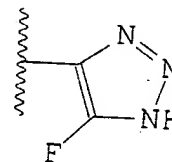
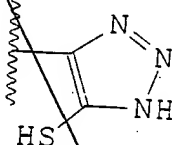
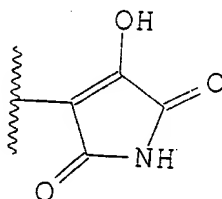
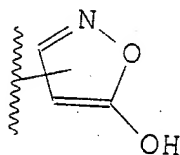
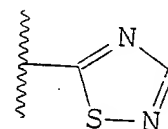
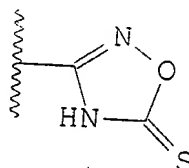
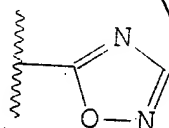
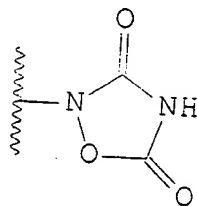
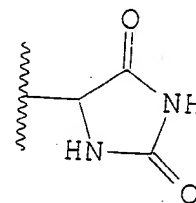
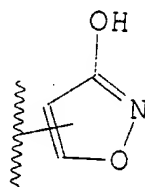
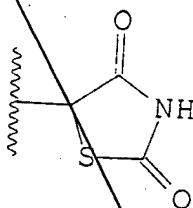
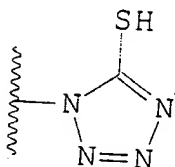
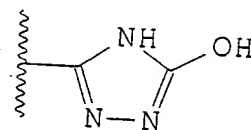
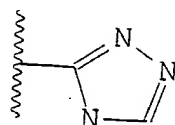
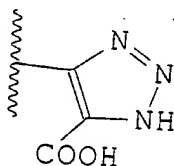
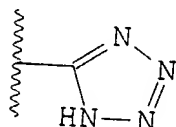
25

10. The pharmaceutical composition of claim 9, wherein R₂ is

a carbocycle or heterocycle containing any combination of CH_2 , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R^3 .

5

11. The pharmaceutical composition of claim 9, wherein R_2 is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

12. The pharmaceutical composition of claim 9, wherein R_2 is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNH₂SO₂R³; -COHNSO₂R³; and -CONR³CN.

13. The pharmaceutical composition of claim 9, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

14. The pharmaceutical composition of claim 8, further comprising a neurotrophic factor different from formula (I).

15. The pharmaceutical composition of claim 14, wherein said neurotrophic factor different from formula (I) is selected from neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3 and neurotrophin 4/5.

16. A method of treating a neurological disorder in an animal, comprising:

administering to the animal an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration.

17. The method of claim 16, wherein the neurological disorder is selected from the group consisting of peripheral

neuropathies cause by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration.

18. The method of claim 16, wherein the neurological disorder is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, amyotrophic lateral sclerosis, and Huntington's Disease.

19. The method of claim 16, wherein the neurological disorder is Alzheimer's disease.

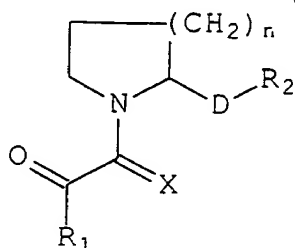
20. The method of claim 16, wherein the neurological disorder is Parkinson's disease.

21. The method of claim 16, wherein the neurological disorder is amyotrophic lateral sclerosis.

22. The method of claim 16, wherein the neurological disorder is Huntington's disease.

23. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

24. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



I

where

n is 1-3;

X is either O or S;

5 R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

10 R₂ is carboxylic acid or a carboxylic acid isostere; and

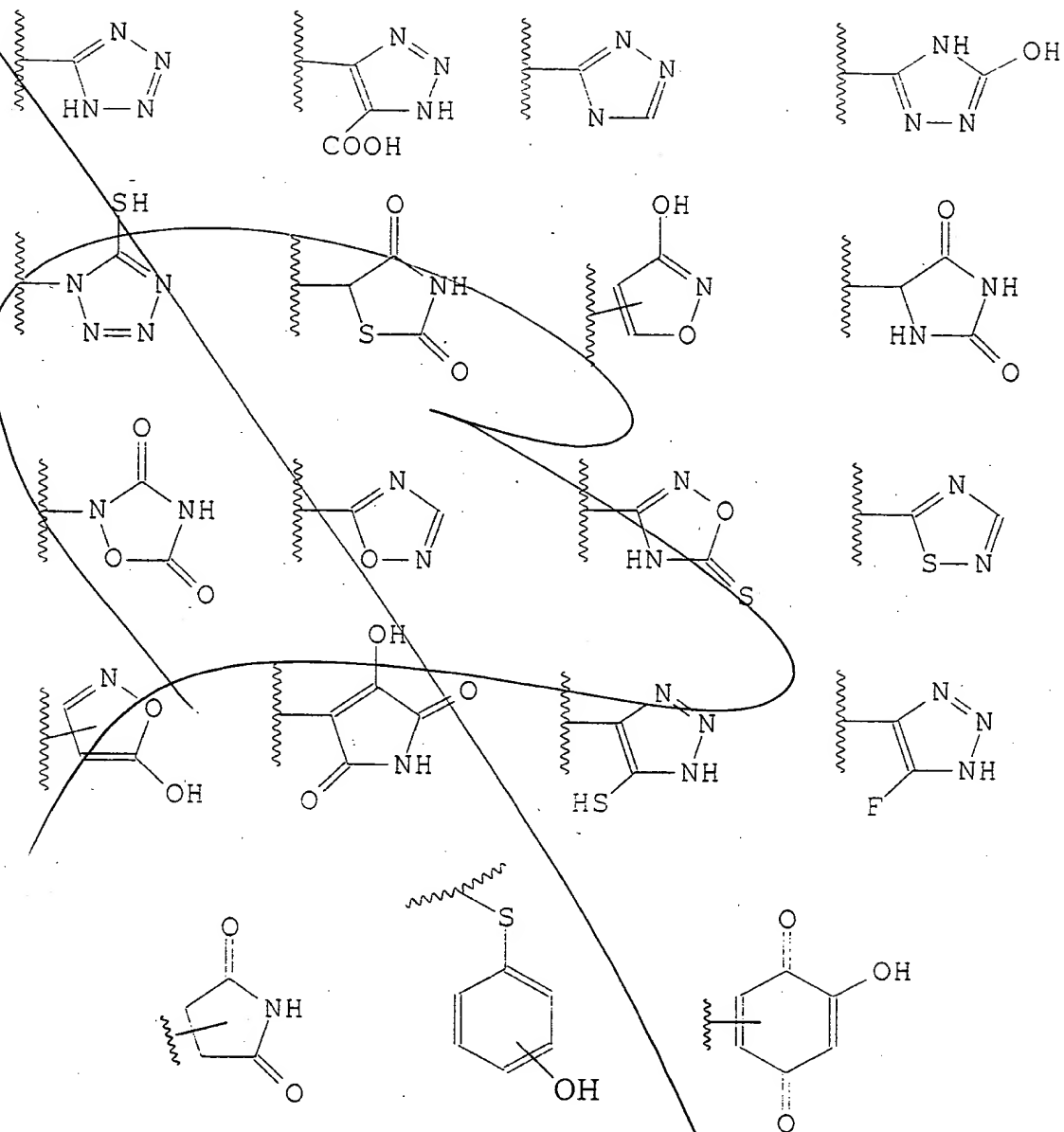
wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R³, where

15 R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, 20 aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate thereof.

25 25. The method of claim 24, wherein R₂ is a carbocycle or heterocycle containing any combination of CH₂, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in 30 one or more positions with R³.

26. The method of claim 24, wherein R₂ is selected from the following group:

Year	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	



where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

27. The method of claim 24, wherein R_2 is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₂(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

28. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

29. The method of claim 16, further comprising administering a neurotrophic factor different from formula (I).

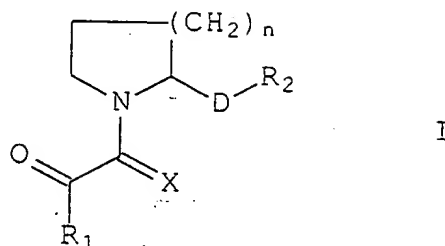
30. The method of claim 29, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

31. A method of stimulating growth of damaged peripheral nerves, comprising:

administering to damaged peripheral nerves an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere to stimulate or promote growth of the damaged peripheral nerves.

32. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

33. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):

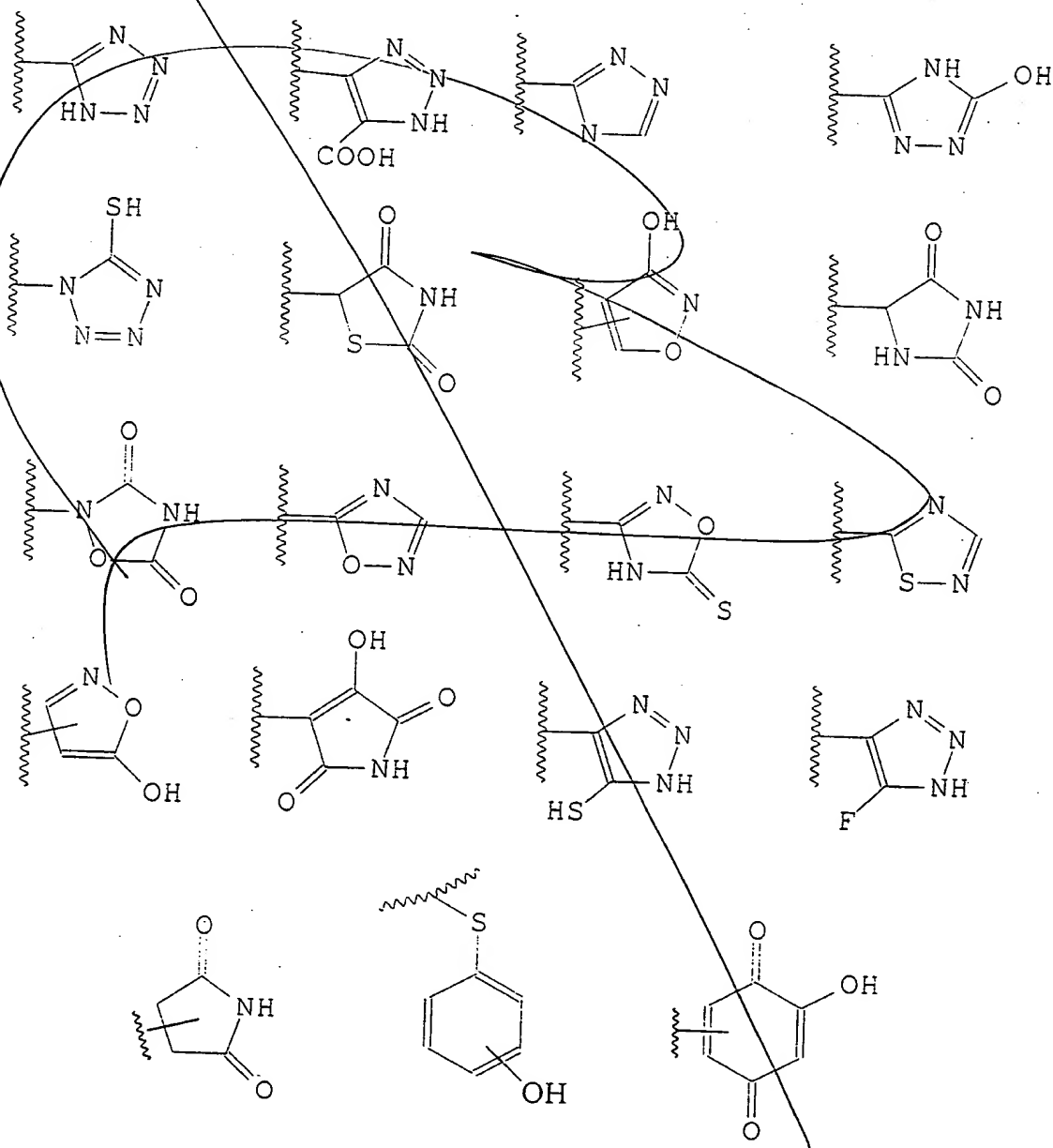


5 where
 n is 1-3;
 X is either O or S;
 R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or
 10 branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;
 D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;
 R₂ is carboxylic acid or a carboxylic acid isostere;
 15 and
 wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R³, where
 R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl,
 20 alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where
 25 R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl;
 or a pharmaceutically acceptable salt, ester, or solvate

thereof.

34. The method of claim 33, wherein R_2 is a carbocycle or heterocycle containing any combination of CH_2 , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R^3 .

35. The method of claim 33, wherein R_2 is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

36. The method of claim 33, wherein R_2 is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

37. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

38. The method of claim 31, further comprising administering a neurotrophic factor different from formula (I).

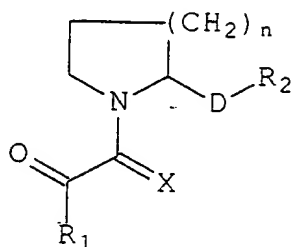
39. The method of claim 38, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

40. A method for promoting neuronal regeneration and growth in animals, comprising:

administering to an animal an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere to promote neuronal regeneration.

41. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

42. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



5 where

n is 1-3;

X is either O or S;

10 R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

15 R₂ is carboxylic acid or a carboxylic acid isostere;

and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R³, where

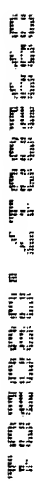
20 R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where

25 R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl;
or a pharmaceutically acceptable salt, ester, or solvate

[illegible]

5

10



where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

45. The method of claim 42, wherein R_2 is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

46. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

47. The method of claim 40, further comprising administering a neurotrophic factor different from formula (I).

48. The method of claim 47, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

49. A method for preventing neurodegeneration in an animal, comprising:

administering to an animal an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere to prevent neurodegeneration.

50. The method of claim 49, wherein the neurodegeneration is Alzheimer's disease.

51. The method of claim 49, wherein the neurodegeneration

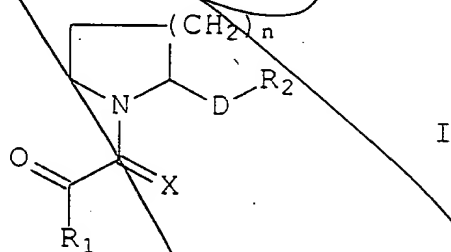
is Parkinson's disease.

52. The method of claim 49, wherein the neurodegeneration is amyotrophic lateral sclerosis.

53. The method of claim 49, wherein the neurodegeneration is Huntington's Disease.

54. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

55. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

X is either O or S;

20 R_1 is selected from the group consisting of C_1-C_9 straight or branched chain alkyl or alkenyl, C_2-C_9 straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

25 D is a bond, or a C_1-C_{10} straight or branched chain alkyl, C_2-C_{10} alkenyl or C_2-C_{10} alkynyl;

R_2 is carboxylic acid or a carboxylic acid isostere;

and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R³, where

R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where R⁷ is hydrogen or C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate thereof.

56. The method of claim 55, wherein R₂ is a carbocycle or heterocycle containing any combination of CH₂, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R³.

57. The method of claim 55, wherein R₂ is selected from the following group:

The image displays 18 chemical structures, primarily nucleobases and nucleosides, each with wavy lines indicating attachment points. A large diagonal line is drawn across the entire set of structures.

- Top Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6, with a COOH group at C2)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Second Row:**
 - Thymine (wavy line at C5, with a methyl group at C5)
 - Adenine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Third Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Fourth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Fifth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Sixth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Seventh Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Eighth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Ninth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)
- Tenth Row:**
 - Adenine (wavy line at C6)
 - Guanine (wavy line at C6)
 - Cytosine (wavy line at C4)
 - Uracil (wavy line at C5)

where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

5 58. The method of claim 55, wherein R_2 is selected from the group consisting of:

-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

10 59. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

15 60. The method of claim 49, further comprising administering a neurotrophic factor different from formula (I).

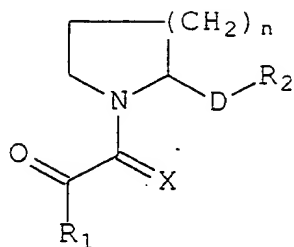
20 61. The method of claim 60, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

25 62. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere.

30 63. The method of claim 62, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

35 64. The method of claim 62, wherein the N-heterocyclic

carboxylic acid or carboxylic acid isostere is a compound of formula (I):



where

n is 1-3;

X is either O or S;

R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

R₂ is carboxylic acid or a carboxylic acid isostere; and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R³, where

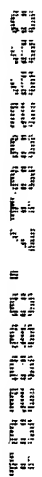
R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where

R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl;

or a pharmaceutically acceptable salt, ester, or solvate

65. The method of claim 64, wherein R_2 is a carbocycle or heterocycle containing any combination of CH_2 , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R^3 .

66. The method of claim 64, wherein R_2 is selected from the
10 following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

5 67. The method of claim 64, wherein R_2 is selected from the group consisting of

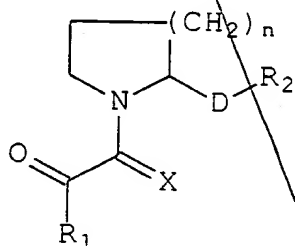
-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

10 68. The method of claim 62, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.

15 69. A pharmaceutical composition comprising:
(i) an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere for treating alopecia or promoting hair growth in an animal; and
(ii) a pharmaceutically acceptable carrier.

20 70. The pharmaceutical composition of claim 69, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

25 71. The composition of claim 69, wherein the carboxylic acid or carboxylic acid isostere is a compound of formula (I):



I

where

n is 1-3;

X is either O or S;

5 R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

10 R₂ is carboxylic acid or a carboxylic acid isostere; and

-- wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R³, where

15 R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, 20 C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate 25 thereof.

72. The composition of claim 71, wherein R₂ is a carbocycle or heterocycle containing any combination of CH₂, O, S, or N in any chemically stable oxidation state, wherein any of the 30 atoms of said ring structure are optionally substituted in one or more positions with R³.

73. The composition of claim 71, wherein R₂ is selected from the following group:

This figure displays a collection of chemical structures for various heterocyclic compounds, primarily purines and pyrimidines, which are common in nucleic acids. Each structure is shown with wavy lines indicating attachment points for polymer chains. The structures include:

- Purine derivatives:**
 - Adenine (top left)
 - Guanine (top middle-left)
 - Hypoxanthine (top middle-right)
 - Xanthine (top right)
 - 2-Mercaptoadenine (middle left)
 - 2-Thiothymine (middle right)
 - 2-Thioadenine (bottom middle-left)
 - 2-Thioguanine (bottom middle-right)
 - 2-Thiothymine (bottom right)
- Pyrimidine derivatives:**
 - Thymine (middle left)
 - Cytosine (middle right)
 - Uracil (bottom left)
 - Thymine (bottom middle-left)
 - Thymine (bottom middle-right)
 - Thymine (bottom right)
- Nucleosides:**
 - Adenosine (middle left)
 - Thymidine (middle right)
 - Uridine (bottom left)
 - Thymidine (bottom middle-left)
 - Thymidine (bottom middle-right)
 - Thymidine (bottom right)

The structures are arranged in a grid-like fashion, with wavy lines indicating attachment points for polymer chains. Some structures are crossed out with diagonal lines, suggesting they are not relevant to the study.

where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

74. The composition of claim 71, wherein R_2 is selected from the group consisting of:

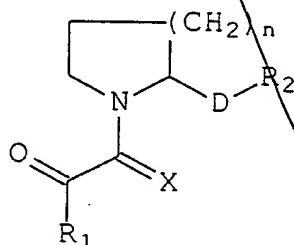
-COOH; -SO₃H; -SO₂HNR³; -PO₂(R³)₂; -CN; -PO₃(R³)₂; -OR³; -SR³; -NHCOR³; -N(R³)₂; -CON(R³)₂; -CONH(O)R³; -CONHNHSO₂R³; -COHNSO₂R³; and -CONR³CN.

75. The composition of claim 69, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.

76. A method for treating a vision disorder, improving vision, treating memory impairment, or enhancing memory performance in an animal, which comprises administering to said animal an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere.

77. The method of claim 76, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

78. The method of claim 76, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is a compound of formula (I):



I

where

n is 1-3;

X is either O or S;

R₁ is selected from the group consisting of C₁-C₉ straight or branched chain alkyl or alkenyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

R₂ is carboxylic acid or a carboxylic acid isostere; and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R³, where

R³ is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ where R⁷ is hydrogen or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate thereof.

79. The method of claim 78, wherein R₂ is a carbocycle or heterocycle containing any combination of CH₂, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R³.

80. The method of claim 78, wherein R₂ is selected from the following group:

[illegible]

where the atoms of said ring structure may be optionally substituted at one or more positions with R^3 .

5 81. The method of claim 78, wherein R_2 is selected from the group consisting of

$-\text{COOH}$; $-\text{SO}_3\text{H}$; $-\text{SO}_2\text{HNR}^3$; $-\text{PO}_2(\text{R}^3)_2$; $-\text{CN}$; $-\text{PO}_3(\text{R}^3)_2$; $-\text{OR}^3$; $-\text{SR}^3$; $-\text{NHCOR}^3$; $-\text{N}(\text{R}^3)_2$; $-\text{CON}(\text{R}^3)_2$; $-\text{CONH}(\text{O})\text{R}^3$; $-\text{CONHNHSO}_2\text{R}^3$; $-\text{COHNSO}_2\text{R}^3$; and $-\text{CONR}^3\text{CN}$.

10 82. The method of claim 76, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.